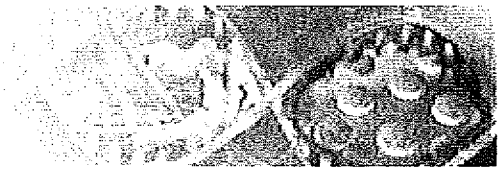
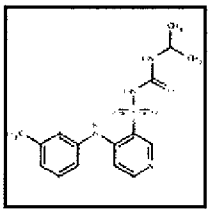
DrugBank



Identification

Name	**Torasemide**
Accession Number	**DB00214** (APRD00217, APRD00295)
Type	small molecule
Groups	approved
Description	Torasemide (rINN) or torsemide (USAN) is a pyridine-sulfonylurea type loop diuretic mainly used in the management of edema associated with congestive heart failure. It is also used at low doses for the management of hypertension. It is marketed under the brand name Demadex. [Wikipedia]

Structure	
	Download: MOL | SDF | SMILES | InChI Display: 2D Structure | 3D Structure
Synonyms	• Torasemida [INN-Spanish] • Torasemidum [INN-Latin] • Torsemide
Brand names	• Demadex • Luprac
Brand name mixtures	Not Available
Categories	• Antihypertensive Agents • Diuretics
CAS number	56211-40-6
Weight	Average: 348.42 Monoisotopic: 348.125611216
InChI Key	InChIKey=NGBFQHCMQULJNZ-UHFFFAOYSA-N
InChI	InChI=1S/C16H20N4O3S/c1-11(2)18-16(21)20-24(22,23)15-10-17-8-7-14(15)19-13-6-4-5-12(3)9-13/h4-11H,1-3H3,(H,17,19)(H2,18,20,21) Plain Text
IUPAC Name	1-{4-[(3-methylphenyl)amino]pyridine-3-sulfonyl}-3-(propan-2-yl)urea
SMILES	CC(C)NC(=O)NS(=O)(=O)C1=C(NC2=CC(C)=CC=C2)C=CN=C1 Plain Text
Mass Spec	Not Available

Taxonomy

Kingdom	Organic
Classes	• Sulfonylureas
Substructures	• Sulfonylureas • Aliphatic and Aryl Amines • Pyridines and Derivatives • Sulfonyls • Benzene and Derivatives • Ureas and Derivatives • Aminopyridines and Derivatives • Heterocyclic compounds • Aromatic compounds • Sulfonamides • Anilines

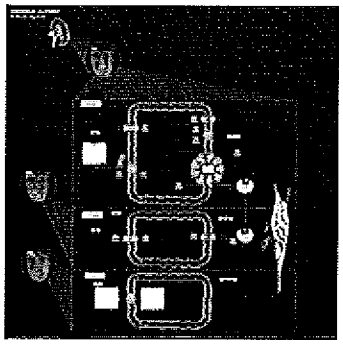
Pharmacology

Indication	For the treatment of edema associated with congestive heart failure, renal disease, or hepatic disease. Also for the treatment of hypertension alone or in combination with other antihypertensive agents.
Pharmacodynamics	Torasemide (INN) or torsemide (USAN) is a novel loop diuretic belonging to pridine sulphonyl urea. It differs form other thiazide diuretics in that a double ring system is incorporated into its structure. Like thiazides, loop diuretics must be secreted into the tubular fluid by proximal tubule cells. In the thick ascending loop Na+ and Cl- reabsorption is accomplished by a $Na^+/K^+/2Cl^-$ symporter. The thick ascending limb has a high reabsorptive capacity and is responsible for reabsorbing 25% of the filtered load of Na^+. The loop diuretics act by blocking this symporter. Because of the large absorptive capacity and the amount of Na^+ delivered to the ascending limb, loop diuretics have a profound diuretic action. In addition, more distal nephron segments do not have the reabsorptive capacity to compensate for this increased load. The osmotic gradient for water reabsorption is also reduced resulting in an increase in the amount of water excreted. Torasemide inhibits the $Na^+/K^+/2Cl^-$-carrier system (via interference of the chloride binding site) in the

Mechanism of action	lumen of the thick ascending portion of the loop of Henle, resulting in a decrease in reabsorption of sodium and chloride. This results in an increase in the rate of delivery of tubular fluid and electrolytes to the distal sites of hydrogen and potassium ion secretion, while plasma volume contraction increases aldosterone production. The increased delivery and high aldosterone levels promote sodium reabsorption at the distal tubules, and By increasing the delivery of sodium to the distal renal tubule, torasemide indirectly increases potassium excretion via the sodium-potassium exchange mechanism. Torasemide's effects in other segments of the nephron have not been demonstrated. Thus torasemide increases the urinary excretion of sodium, chloride, and water, but it does not significantly alter glomerular filtration rate, renal plasma flow, or acid-base balance. Torasemide's effects as a antihypertensive are due to its diuretic actions. By reducing extracellular and plasma fluid volume, blood pressure is reduced temporarily, and cardiac output also decreases.
Absorption	Rapidly absorbed following oral administration. Absolute bioavailability is 80%. Food has no effect on absorption.
Volume of distribution	• 12 to 15 L [normal adults or in patients with mild to moderate renal failure or congestive heart failure]
Protein binding	> 99%
Metabolism	Metabolized via the hepatic CYP2C8 to 5 metabolites. The major metabolite, M5, is pharmacologically inactive. There are 2 minor metabolites, M1, possessing one-tenth the activity of torasemide, and M3, equal in activity to torasemide. Overall, torasemide appears to account for 80% of the total diuretic activity, while metabolites M1 and M3 account for 9% and 11%, respectively.
Route of elimination	Torsemide is cleared from the circulation by both hepatic metabolism (approximately 80% of total clearance) and excretion into the urine (approximately 20% of total clearance in patients with normal renal function).
Half life	3.5 hours
Clearance	Not Available
Toxicity	Symptoms of overdose include dehydration, hypovolemia, hypotension, hyponatremia, hypokalemia, hypochloremic alkalosis, and hemoconcentration. Oral LD_{50} in rat is 5 g/kg, and intravenous LD_{50} in rat is 500 mg/kg.
Affected organisms	• Humans and other mammals

Enzyme	Metabolite	Reaction	K_m	V_{max}
Prostaglandin G/H synthase 1		hydroxylation		
Cytochrome P450 2C9		methyl-hydroxylation		
Cytochrome P450 2C9	hydroxytorsemide	tolylmethylhydroxylation	11.9	136.61
Cytochrome P450 2C8	hydroxytorsemide	tolylmethylhydroxylation	147	32.22

Pathways

Pathway	Name	SMPDB ID
	Torsemide Pathway	SMP00118

Pharmacoeconomics

Manufacturers

- Hoffmann la roche inc
- Bedford laboratories
- Luitpold pharmaceuticals inc
- Meda pharmaceuticals inc
- Apotex inc etobicoke site
- Aurobindo pharma ltd
- Hetero drugs ltd
- Par pharmaceutical inc

- Pliva pharmaceutical industry inc
- Roxane laboratories inc
- Sun pharmaceutical industries ltd
- Teva pharmaceuticals usa inc

Packagers

- American Regent
- Apotex Inc.
- Aurobindo Pharma Ltd.
- Camber Pharmaceuticals Inc.
- Cardinal Health
- Diversified Healthcare Services Inc.
- F Hoffmann-La Roche Ltd.
- General Injectables and Vaccines Inc.
- Greenstone LLC
- Heartland Repack Services LLC
- Hetero Drugs Ltd.
- Ivax Pharmaceuticals
- Mckesson Corp.
- Meda AB
- Murfreesboro Pharmaceutical Nursing Supply
- Neuman Distributors Inc.
- Palmetto Pharmaceuticals Inc.
- Par Pharmaceuticals
- Physicians Total Care Inc.
- Pliva Inc.
- Preferred Pharmaceuticals Inc.
- Prepak Systems Inc.
- Resource Optimization and Innovation LLC
- Roxane Labs
- Sun Pharmaceutical Industries Ltd.
- Teva Pharmaceutical Industries Ltd.
- UDL Laboratories
- Vangard Labs Inc.

Dosage forms

Form	Route	Strength
Injection, solution	Intravenous	
Tablet	Oral	

Prices

Unit description	Cost	Unit
Demadex 100 mg tablet	5.69 USD	tablet
Torsemide 100 mg tablet	3.16 USD	tablet
Demadex 20 mg tablet	1.59 USD	tablet
Demadex 10 mg tablet	1.39 USD	tablet
Demadex 5 mg tablet	1.28 USD	tablet
Torsemide 20 mg tablet	0.85 USD	tablet
Torsemide 10 mg tablet	0.73 USD	tablet
Torsemide 5 mg tablet	0.66 USD	tablet

Patents: Not Available

Properties

State: solid

Melting point: 164-164 oC

Experimental Properties

Property	Value	Source
water solubility	Water soluble	PhysProp
logP	2.3	PhysProp
pKa	7.1	Various sources

Property	Value	Source
water solubility	5.96e-02 g/l	ALOGPS